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BRIEF REPORT

Photodynamic Therapy for Barrett's Esophagus: Cardiac Effects

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Background and Objective: **Atrial fibrillation has been reported following esophageal photodynamic therapy. This study presents the results of serial cardiac testing following photodynamic therapy for patients with Barrett's esophagus and with dysplasia or early carcinoma.**
Study Design/Materials and Methods: **Twelve patients were treated using photodynamic therapy. Serum creatinine phosphokinase and lactic dehydrogenase isoenzyme levels were determined pretreatment and 24, 48, and 72 hours after treatment. Electrocardiograms were obtained before and 48 hours after treatment. A rhythm strip was obtained 1 week posttreatment. Clinical assessment for cardiac arrhythmias occurred daily following therapy.**
Results: **Transient atrial fibrillation was noted in one patient during a follow-up endoscopy. However, no significant or permanent abnormality was noted in cardiac enzymes or electrocardiograms.**
Conclusion: **No permanent electrocardiographic changes or significant abnormalities in cardiac enzymes were detected following esophageal photodynamic therapy in patients with or without histories of cardiac disease. Delivery of esophageal PDT is not associated with permanent adverse cardiac effects. Lasers Surg. Med. 21:317–320, 1997.** **© 1997 Wiley-Liss, Inc.**

Key words: dysplasia; esophageal cancer

INTRODUCTION

Barrett's esophagus is associated with an increased occurrence of mucosal dysplasia and adenocarcinoma in the specialized glandular mucosa in this disease [1–13]. Photodynamic therapy (PDT) has been used successfully to destroy mucosal dysplasia and early esophageal cancer in patients with Barrett's esophagus [14–17]. PDT, however, produces marked mucosal destruction with associated short-term chest discomfort and dysphagia. Atrial fibrillation has been reported following esophageal PDT [15].

This study evaluates serial cardiac enzymes and electrocardiograms following esophageal PDT.

MATERIALS AND METHODS

Twelve patients referred for PDT had repeated endoscopic examinations and biopsies demonstrating Barrett's esophagus and dysplasia (Table 1). One (1) patient had an early cancer <1.0 cm in size (T1). In patients with biopsy-proven adenocarcinomas, only those with lesions that were interpreted Tis-1, N-0, M-0 [18] by endoscopic ultrasound [19] and computed tomography

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TABLE 1. Cardiac Effects Following Esophageal Photodynamic Therapy

Age, race, sex	Cardiac disease[a]	Dysplasia or cancer[b]	Level of PDT Tx[c]	Enzyme change after Tx	EKG change after Tx
63 WM	None	HG	24–33	NC	NC
42 WM	None	HG	25–35	NC	NC
64 WM	None	HG	30.5–36	NC	NC
57 WM	None	LG	31–36	NC	NC
53 WM	None	HG	26–36	NC	NC
55 WM	None	HG	22–27.5	NC	NC
72 WM	CAD	HG	25–33	NC	NC
79 WM	CAD	HG	24–33	NC	NC
68 WF	CAD	HG	33.5–39	NC	NC
81 WM	CAD	HG, T1	28–37	NC	NC
73 WF	CAD	HG	20–30	NC	NC
55 WM	Heart transplant	HG	28.5–39	NC	NC

[a]CAD = coronary artery disease. PDT treatment area, cm from dental margin.
[b]HG = high grade dysplasia; LG = low grade dysplasia; T1 = cancer limited to mucosa and submucosa.
[c]Tx = PDT treatment area, cm from dental margin. NC = no change.

were included in the study. Six patients had no evidence of cardiac disease, whereas five had coronary artery disease and one was a heart transplant patient. The study was approved by the Institutional Review Board of the Thompson Cancer Survival Center.

Following informed consent, porfimer sodium 2 mg/Kg (Photofrin® Quadra Logics Technologies, Vancouver, BC, Canada) was injected intravenously. Forty-eight hours later, 630 nm light was endoscopically delivered using a 2.0 or a 2.5 cm cylindrical diffuser. An argon-pumped dye-laser (Lambda Plus, Coherent, Palo Alto, CA) tuned to a wavelength of 630 nm was used to provide endoscopic delivery of the red light to the esophagus. The wavelength was verified using an optical multichannel analyzer system, OMA III (EG&G Princeton Applied Research, Princeton, NJ). The light was focused into a 200 μm extension fiber. A 400 μm 2.0 or 2.5 cm cylindrical diffuser was attached to the extension fiber. The diffuser was inserted through the endoscope into the esophageal lumen to deliver light intraluminally to the targeted area. Power density was 400 mW/cm of diffuser with a treatment time providing energy density of 250 Joules/cm from the diffuser. The power delivered from the cylindrical diffuser was measured using an integrating sphere power meter (model 2010; PDT Systems, Santa Barbara, CA) calibrated at 630 nm.

All patients were sedated with meperidine and midazolam during endoscopic procedures. Oxygen was administered by nasal catheter at 2–3 l/min during treatment. Endoscopies were performed with the Fujinon EVG-CT and EVG-FP (Wayne, NJ). In all patients, careful endoscopic measurements from the dental margin were obtained precisely to determine the location for PDT delivery. A follow-up endoscopy was performed at 48 hours to determine if additional light treatment was required. During this follow-up exam, eight patients (cases #2–4,6,7,9,11,12) underwent a second light treatment to residual tumor tissue or to small areas of esophageal mucosa that were not significantly damaged from the initial PDT treatment. A range of 5–10.5 cm of esophageal mucosa was treated. All patients were treated with omeprazole, 20 mg twice a day. All were treated as outpatients and received intermittent intravenous fluids for 5–7 days following PDT.

Serum creatine kinase (CPK) (Baxter Diagnostics, Deerfield, IL) and CPK-MB (Hybritech, San Diego, CA) enzymes, lactate dehydrogenase (LDH) (Baxter Diagnostics) and LDH isoenzymes (Beckman Instruments, Fullerton, CA) levels were determined prior to PDT and 24, 48, and 72 hours following treatment. EKGs were done at baseline and 48 hours following PDT. Patients were visited daily for 1 week following PDT and clinically assessed for cardiac arrhythmias. An EKG rhythm tracing was performed 1 week following PDT.

RESULTS

Full dose (300 J/cm) PDT treatment administered to >3–4 cm of esophagus produced moderate chest pain and dysphagia lasting for 5–7 days, but this gradually improved in all patients. Extensive injury to the treated mucosa was observed along with destruction of dysplastic epithelium and superficial (T1) cancer.

Total CPK and CPK-MB enzymes, LDH and

LDH isoenzymes measured prior to PDT and at 24, 48, and 72 hours after PDT demonstrated no enzymatic evidence of myocardial injury. EKGs taken before and 48 hours after PDT demonstrated no permanent electrocardiographic changes. One transient rhythm abnormality (atrial fibrillation) occurred during the 48-hour endoscopic follow-up in an 81-year-old patient (≠10). However, sinus rhythm had returned before the end of the procedure without specific therapy. No rhythm change was noted clinically in any patient during daily visits over a 1 week time period following PDT. All rhythm strips 1 week after PDT demonstrated no significant change compared to baseline studies.

DISCUSSION

Photodynamic therapy represents a minimally invasive endoscopic treatment resulting in the elimination of Barrett's mucosal dysplasia and the reduction of Barrett's mucosa. PDT provides an alternative to esophagectomy for patients with Barrett's esophagus and dysplasia and for selected patients with T1 carcinoma [14–17].

Atrial fibrillation has been reported following PDT [15], raising concerns about the possibility of myocardial injury associated with the treatment. This report details cardiac effects in 12 patients treated with PDT for dysplasia or early esophageal adenocarcinoma in Barrett's esophagus. Extensive mucosal destruction was observed after PDT. The long-term follow-up on these patients is part of an ongoing clinical trial in our institution.

Atrial fibrillation was transiently seen during a follow-up endoscopic procedure in one of our patients. However, this study of 12 consecutive patients, six of whom had a definite history of cardiac disease, demonstrated that esophageal PDT does not result in significant myocardial injury or permanent rhythm disturbance. CPK and CPK-MB and LDH isoenzymes 24, 48, and 72 hours following PDT remained within normal laboratory ranges. EKGs 48 hours posttreatment and rhythm tracings 1 week posttherapy remained similar to pretreatment studies.

Atrial fibrillation reported previously [15] possibly resulted from deep injury and resulting peri-esophagitis following esophageal PDT delivered at the level of the atrium. However, all of the 12 patients reported in this study received esophageal PDT delivered in part at the level of the atrium. No permanent cardiac rhythm disturbances were observed in spite of significant esophageal injury observed following PDT.

In summary, no enzymatic evidence of myocardial injury or permanent rhythm disturbance was noted in 12 consecutive patients undergoing extensive esophageal PDT for Barrett's esophagus with dysplasia or early esophageal cancer. We conclude that the delivery of esophageal PDT is not associated with permanent adverse cardiac effects.

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